Influence of preoperative renal dysfunction on one-year bypass graft patency and two-year outcomes in patients undergoing coronary artery bypass surgery

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Objective: Limited information exists on the impact of preoperative renal dysfunction on internal thoracic artery and saphenous vein graft failure and 2-year clinical outcomes in patients undergoing coronary artery bypass surgery.

Methods: We studied the impact of preoperative renal dysfunction (creatinine clearance < 60 mL/min) on 1-year internal thoracic artery and saphenous vein graft failure (defined as ≥ 75% angiographic stenosis) and 2-year clinical events (death; death or myocardial infarction; and death, myocardial infarction, or revascularization) in 3014 patients undergoing coronary artery bypass surgery enrolled in the Project of Ex-vivo Vein Graft Engineering via Transfection-IV study.

Results: Of 2973 patients (98.6%) with preoperative measurement of renal function, 440 (14.8%) had renal dysfunction. Most baseline comorbidities were higher in these patients. Two-year clinical events were higher in patients with preoperative renal dysfunction (adjusted death, myocardial infarction, or revascularization, hazard ratio 1.21, 95% confidence interval 0.97–1.50; adjusted death or myocardial infarction, hazard ratio 1.35, 95% confidence interval 1.05–1.74; adjusted death, hazard ratio 1.47, 95% confidence interval 0.98–2.21). However, saphenous vein graft (odds ratio 1.02, 95% confidence interval 0.79–1.33) and internal thoracic artery (odds ratio 0.76, 95% confidence interval 0.40–1.44) failure were similar in the 2 groups.

Conclusion: Although the risk of adverse clinical events is higher in patients with preoperative renal dysfunction, that of internal thoracic artery and saphenous vein graft failure is not. This suggests that factors other than graft failure account for the worse clinical outcomes in this high-risk cohort. Further studies are needed to identify other mechanisms of these worse outcomes so that appropriate measures can be developed to improve long-term outcomes in patients with renal dysfunction undergoing coronary artery bypass surgery.

Renal insufficiency in patients undergoing coronary artery bypass graft (CABG) surgery has been shown to be associated with high short-term morbidity and mortality, and increased resource use.[1-4] However, the influence of preoperative renal dysfunction on short- and long-term graft patency and its relationship to outcomes of patients undergoing CABG at a wide range of hospitals is less well known.

The goal of the present investigation was to evaluate the impact of preoperative renal dysfunction on in-hospital and 2-year clinical outcomes and 1-year angiographic outcomes in patients undergoing CABG using data from the Project of Ex-vivo Vein Graft Engineering via Transfection (PREVENT)-IV study.[5,6] We hypothesized that renal dysfunction before CABG would be associated with increased short-term morbidity and mortality and that this elevated risk would persist beyond the acute phase and be observed at the 2-year follow-up. In addition, we theorized that these worse outcomes were, at least in part, mediated through higher rates of graft failure in this high-risk group.

MATERIALS AND METHODS

PREVENT-IV Trial and Patient Population

The details of PREVENT-IV trial have been published.[5,6] In brief, PREVENT-IV was a phase 3, multicenter, randomized, double-blind, placebo-controlled trial to assess the efficacy of edifoligide an oligonucleotide decoy that binds to and inhibits E2F transcription factors and is thereby thought to prevent neointimal hyperplasia and vein graft failure. A total of 3014 patients undergoing primary CABG surgery with at least 2 planned vein grafts at 107 sites in the United States were randomly assigned between August of 2002 and October of 2003 to ex vivo autologous vein graft treatment with either edifoligide or placebo before implantation of these conduits. The first 2400 patients enrolled were assigned to an angiographic cohort and scheduled to return for angiography 12 to 18 months after surgery. Major exclusion criteria included previous cardiac surgery or planned concomitant valve surgery (because of the increased early mortality associated with these procedures), vasculitis or another nonatherosclerotic cause of coronary artery disease, hypercoagulable state, involvement in another investigational drug or device study within 30 days, or a comorbid illness that would

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Abbreviations and Acronyms

CABG = coronary artery bypass graft
CK = creatine kinase
ITA = internal thoracic artery
MI = myocardial infarction
PREVENT-IV = PRoject of Ex-vivo Vein Graft Engineering via Transfection-IV
SVG = saphenous vein graft
ULN = upper limit of normal

make 5-year survival unlikely. Institutional review board approval was obtained at all sites, and all patients gave written informed consent before participation. For the purpose of this analysis, we included all patients enrolled in the PREVENT-IV study. Creatinine clearance was determined as [(140–age) * weight)/(72 * creatinine)] * 0.85 if the patient was female.[7] Preoperative renal dysfunction was defined as creatinine clearance less than 60 mL/min.

Outcome Measures

The main angiographic outcome measure for this analysis was vein graft failure, defined as a stenosis of 75% or greater in at least 1 vein graft assessed by quantitative coronary angiography 12 to 18 months after surgery in patients who underwent follow-up angiography. Patients in the angiographic cohort who underwent angiography for clinical reasons before 12 months and met the above end point did not have additional protocol angiography. Patients who died before angiography were not included in the angiographic end point. Secondary angiographic end points included (1) per graft incidence of vein graft failure (≥75% stenosis and vein graft occlusion) and (2) per graft incidence of vein graft occlusion. All angiograms in PREVENT-IV were interpreted at the PERFUSE Angiographic Core Laboratory (Boston, Mass), using standard quantitative coronary angiographic techniques. The main clinical end point for this analysis is the composite of death, myocardial infarction (MI), or repeat revascularization at 2 years.

In PREVENT-IV trial, patients were contacted via mail or telephone at 6 and 9 months and at 1 year after CABG surgery. Annual follow-up is ongoing and planned at 2, 3, 4, and 5 years after CABG surgery. Two-year follow-up is complete at this time. For those who reported a possible MI or revascularization procedure, additional medical records were obtained from their hospitals. All suspected MIs and revascularization procedures were adjudicated by a blinded, independent clinical events committee using prespecified criteria. Perioperative MI was defined as a creatine kinase-MB (CK-MB) fraction of greater than 10 times the upper limit of normal (ULN) or greater than 5 times the ULN with new Q waves longer than 30 ms in 2 contiguous leads or, if postoperative CK-MB samples were not available, new Q waves longer than 30 ms in 2 contiguous leads. Perioperative MI was diagnosed if CK-MB was elevated within 24 hours of surgery when there was not an interval clinical event and when the elevation was not attributable to a preoperative MI. Postoperative MI was defined as either spontaneous (CK-MB > 2 times the ULN or new Q waves > 30 ms in 2 contiguous leads), after percutaneous coronary intervention (CK-MB > 3 times the ULN or new Q waves > 30 ms in 2 contiguous leads), or after CABG surgery (CK-MB > 10 times the ULN or > 5 times the ULN with new Q waves > 30 ms in 2 contiguous leads). For patients for whom CK-MB samples and electrocardiograms were not available, MI could be defined by the presence of ''myocardial infarction,'' ''heart attack,'' or similar term in the medical record documenting that an MI had occurred after the initial CABG procedure. Postprocedure acute renal dysfunction was defined as an increase of 50% or more and/or 0.7 mg/dL or more in preprocedure serum creatinine or serum creatinine more than 2.0 mg% or requirement for dialysis after the CABG.

Statistical Analysis

All analyses were performed with SAS software (SAS Inc, Cary, NC). Baseline characteristics, surgery, and hospital care characteristics were summarized in terms of frequencies and percentages for categoric variables and by the median, 25th, and 75th percentiles for continuous variables. Differences in characteristics between patients with and without preoperative renal dysfunction were assessed using the Wilcoxon rank-sum test (for continuous variables) and the chi-square or Fisher's exact test (for categoric variables). All tests of significance were 2-tailed.

Cumulative event rates for the main adverse coronary event outcomes were calculated by the Kaplan–Meier method. The statistical significance of differences in outcomes between the 2 groups was assessed with the log-rank test. In addition, covariate adjusted analyses of outcomes were assessed using the Cox proportional hazards model. Covariates adjusted for included age, gender, history of congestive heart failure, recent MI (within 30 days before enrollment), and use of an internal thoracic artery (ITA) conduit. Hazard ratios and 95% confidence intervals were calculated with the Cox model.

For the per graft end points of 75% or greater stenosis and occlusion, general estimating equation techniques were used to adjust for correlation between grafts within a patient. Covariates adjusted for included weight, duration of surgery, harvest technique, target artery quality, and whether it was a composite graft.

RESULTS

Baseline Characteristics, Surgical Features, and In-hospital Care

Of 2973 patients (98.6% of the PREVENT-IV population) with preoperative measurement of renal function, 440 (14.8%) had preoperative moderate (creatinine clearance 30 to <60 mL/min, 419 [14.1%]) or severe (creatinine clearance < 30 mL/min, 21 [0.7%]) renal dysfunction (Tables 1 and 2). Mild renal dysfunction (creatinine clearance 60 to <90) was present in more than one third of patients (n = 1115 [37.5%]). No patient on dialysis before CABG was enrolled in the PREVENT-IV study. Table 1 shows the baseline characteristics of the 2 groups. The median age of patients with preoperative renal dysfunction was 11 years older than patients without renal dysfunction. These patients were more likely to be women and non-white. Similarly, the median weight was 17 kg lower and height was 7 cm shorter in patients with preoperative renal dysfunction than those without preoperative renal dysfunction. Most comorbid conditions, including hypertension, chronic lung disease, prior congestive heart failure, prior stroke, and prior peripheral and cerebrovascular disease, were higher in patients with preoperative renal dysfunction than in those without preoperative renal dysfunction. These patients had higher systolic and lower diastolic blood pressure. No differences were noted in the prevalence of diabetes, hyperlipidemia, prior MI, New York Heart Association class, and number of diseased vessels or left ventricular ejection fraction.

The median number of saphenous vein grafts (SVGs) per patient did not differ between the 2 groups. In contrast, the proportion of patients receiving an ITA graft was lower for the preoperative renal dysfunction group. In addition, the quality of target vessels (graded as good, fair, and poor)

TABLE 1. Baseline characteristics

Characteristics	Overall	No renal dysfunction	Preoperative renal dysfunction	*P* value
N	2973	2533	440	
Age, median (IQR), y	64 (56–71)	62 (55–68)	73 (68–76)	<.001
Female sex	20.9%	17.4%	40.7%	<.001
Race nonwhite	8.9%	8.5%	11.1%	.028
Weight (median [IQR]), kg	88 (77–100)	90 (79–102)	73 (64–83)	<.001
Height (median [IQR]), cm	175 (168–180)	175 (168–180)	168 (160–175)	<.001
Medical history				
Hypertension	75.0%	73.8%	81.6%	.001
Diabetes mellitus	37.6%	37.7%	37.0%	.781
Current smoking	22.7%	24.1%	15.0%	<.001
Hyperlipidemia	76.2%	76.6%	74.3%	.304
Chronic lung disease	15.6%	14.9%	19.8%	.010
Preoperative atrial	7.1%	6.4%	10.7%	.001
Fibrillation/flutter				
MI, any	42.1%	41.8%	43.9%	.411
MI within 3 mo	21.7%	21.8%	21.1%	.772
Prior percutaneous coronary interventions	25.8%	26.1%	23.9%	<.001
Congestive heart failure	9.4%	8.2%	16.1%	<.001
Prior stroke	5.4%	4.6%	10.2%	<.001
Peripheral vascular disease	12.3%	11.0%	20.0%	<.001
Cerebrovascular disease	12.6%	10.8%	23.2%	<.001
History of liver disease	1.8%	1.7%	2.0%	.652
Cardiogenic shock	0.8%	0.8%	1.1%	.386
Presenting features				
Presenting heart rate (median [IQR]), beats/min	70 (62–80)	70 (62–80)	70 (60–80)	.285
Presenting SBP (median [IQR]), mm Hg	134 (120–149)	133 (120–148)	137 (123–154)	<.001
Presenting DBP (median [IQR]), mm Hg	75 (67–82)	75 (68–82)	73 (64–80)	.002
Peoperative NYHA class				.374
I	40.2%	40.7%	37.3%	
II	33.4%	33.3%	33.8%	
III	18.0%	17.9%	18.8%	
IV	8.4%	8.1%	10.2%	
Left ventricular ejection fraction, median (IQR)	50% (40%–60%)	50% (40%–60%)	55% (45%–60%)	.239
No. of diseased vessels $\geq$ 2 or left main (>50% stenosis)	79.4%	79.3%	80.2%	.785
Baseline creatinine median (IQR), mg/dL	1.0 (0.9–1.2)	1.0 (0.9–1.1)	1.4 (1.1–1.6)	<.001
Creatinine clearance, median (IQR), mL/min	94 (78–117)	51 (43–56)	88 (70–112)	<.001

IQR, Interquartile range; *MI,* myocardial infarction; *SBP,* systolic blood pressure; *DBP,* diastolic blood pressure, *NYHA,* New York Heart Association.

was similar in the 2 cohorts. Although there were no differences in the 2 groups in the duration of surgery or cardiopulmonary bypass, postoperative duration on ventilator and length of stay in the intensive care unit and hospital were significantly longer in the preoperative renal failure group. Although the overall use of some medications (particularly aspirin, beta-blockers, and statins) was lower in the preoperative renal dysfunction group, this did not differ between the 2 groups among eligible patients without contraindications (data not shown).

Angiographic Results

In the overall PREVENT-IV population, the proportions of patients assigned to the angiographic cohort were similar among patients with and without renal dysfunction (n = 350 [80%] and 2020 [80%], respectively) (Table 3). Within the cohort that was scheduled to return for angiographic follow-up, however, the proportion that actually returned for angiography was lower among patients with renal dysfunction than patients without renal dysfunction (62% vs 79%). The number of patients who died before 18 months without an angiogram was higher among patients with renal dysfunction than patients without renal dysfunction (70% vs 82%).

One-year follow-up angiography revealed no differences in the adjusted rates of SVG or ITA failure (defined as stenosis $\geq$ 75%) or occlusion between the 2 groups (Figure 1). There was also no interaction between treatment assignment and renal dysfunction on vein graft failure in multivariate analysis. Similarly, when the analysis was performed focusing on per patient end points, the proportion of patients with failure or occlusion of 1 or more SVGs or ITA stenosis of

TABLE 2. Surgery and hospital care

Characteristics	Overall	No renal dysfunction	Preoperative renal dysfunction	*P* value
N	2973	2533	440	
Urgent/emergency/emergency salvage surgery	51.4%	52.3%	46.4%	.136
ITA graft	92.5%	93.2%	88.2%	<.001
Surgery duration, median (IQR), min	231 (193–272)	231 (193–272)	230 (193–270)	.578
Cardiopulmonary bypass	78.9%	79%	78%	.608
Duration of cardiopulmonary bypass, median (IQR), min	100 (79–122)	100 (79–123)	97 (80–122)	.744
Postoperative duration, median (IQR)				
Ventilator, h	7.5 (4.5–13.5)	7.0 (4.5–13.0)	9.0 (5.5–16.0)	<.001
Intensive care unit stay, h	26 (22–47)	25.0 (22.0–46.0)	29.0 (23.0–65.0)	<.001
Hospital stay, d	6.0 (5.0–8.0)	6.0 (5.0–8.0)	7.0 (6.0–9.0)	<.001
No. of treatment eligible vein grafts	2.0 (2.0–3.0)	2.0 (2.0–3.0)	2.0 (2.0–3.0)	.389
Worst target artery quality				.817
Good	43.0%	43.2%	41.9%	
Fair	35.9%	35.8%	36.0%	
Poor	21.1%	20.9%	22.1%	
Medications continued at 30 d				
Aspirin	90.5%	91.0%	88.0%	.055
Thienopyridine	21.8%	21.6%	23.0%	.507
ACE inhibitor	35.8%	36.3%	32.6%	.140
Angiotensin II receptor blocker	6.8%	6.3%	9.4%	.018
Beta-blockers	78.8%	79.5%	74.9%	.031
HMG-CoA reductase inhibitor	72.8%	73.4%	69.2%	.067

ITA, Internal thoracic artery; *IQR,* interquartile range; *ACE,* angiotensin-converting enzyme.

75% or more or with complete SVG or ITA occlusion did not differ between the 2 groups (data not shown). In addition, even when we assumed that all patients who died had vein graft failure, there was no difference in vein graft failure between the 2 groups (odds ratio 1.20, 95% confidence interval 0.92–1.57, $P = .18$). Finally, because the patency of grafts would depend on the quality of the vessel on which they are anastomosed to, we performed a sensitivity analysis restricting our angiographic end points only to SVG and ITA attached to a good target vessel. This analysis also failed to reveal any difference in the rate of SVG or ITA failure or occlusion between the 2 groups.

Clinical Events

Of the clinical events evaluated in the PREVENT-IV study through 30 days, many were more frequent in patients with than in those without preoperative renal dysfunction (Table 4). Most notably, the incidence of pneumonia was 1.8-fold higher, mortality was 3-fold higher, acute renal failure was 3.5-fold higher, and the need for postoperative dialysis was 4-fold higher in patients with preoperative renal dysfunction.

Two-year major adverse cardiac events are shown in Table 5 (Figure 2). The incidence of the combined end point of death or MI was significantly higher in patients with

TABLE 3. Angiographic results

	Preoperative renal dysfunction		Unadjusted		Adjusted*	
Per graft angiographic end points	**Yes (n = 508)**	**No (n = 3735)**	**Odds ratio (95% CI)**	***P***	**Odds ratio (95% CI)**	***P***
SVG stenosis ≥ 75%	26.6%	25.1%	1.08 (0.63–1.38)	.5569	1.02 (0.79–1.33)	.8673
SVG occlusion	24.0%	22.0%	1.10 (0.85–1.43)	.4472	1.04 (0.79–1.36)	.7816
Grafts with ''good'' target arteries	(n = 333)	(n = 2377)				
SVG stenosis ≥ 75%	20.4%	22.3%	0.92 (0.67–1.26)	.5965	0.81 (0.58–1.13)	.2109
SVG occlusion	18.0%	19.7%	0.92 (0.66–1.28)	.6327	0.80 (0.56–1.13)	.2001
ITA graft-Total	(n = 172)	(n = 1405)				
ITA stenosis ≥ 75%	6.4%	8.3%	0.76 (0.40–1.44)	.3974	-	-
ITA occlusion	1.7%	3.9%	0.45 (0.14–1.47)	.1863	-	-
ITA with ''good'' target arteries	(n = 122)	(n = 940)				
ITA stenosis ≥ 75%	7.4%	8.6%	0.84 (0.41,1.71)	.6256	-	-
ITA occlusion	2.5%	4.0%	0.60 (0.18,1.97)	.3983	-	-

CI, Confidence interval; *SVG,* saphenous vein graft; *ITA,* internal thoracic artery. *Adjusted for weight, duration of surgery, harvest technique, target vessel quality, and composite grafts.

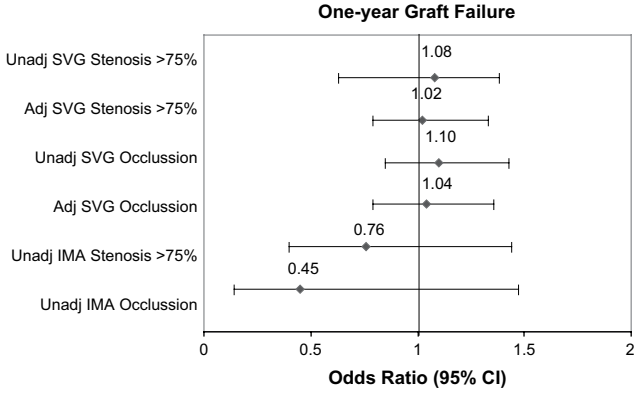

FIGURE 1. Unadjusted and adjusted clinical events in patients with preoperative renal dysfunction compared with those with no preoperative renal dysfunction.

preoperative renal dysfunction. After adjustment for differences in prognostically important baseline variables and differences in ITA use, the preoperative renal dysfunction cohort continued to demonstrate a significant 34% increased risk of death or MI at 2 years follow-up. Similar trends were noted for increased risks of the composite of death, MI, or revascularization and for death at 2 years with 19% and 47% higher risks of these events, respectively, in the preoperative renal dysfunction group.

DISCUSSION

Patients with varying degree of renal dysfunction constitute an increasing proportion of those undergoing CABG.[1-4] This escalating trend is the result of the increased risk of cardiovascular disease in patients with even mild renal dysfunction[8,9] attributed to the high prevalence of risk factors, such as hypertension, diabetes, smoking, dyslipidemia, peripheral vascular disease, and advanced age.[1,10] Multiple studies have confirmed that CABG is associated with increased risk of mortality and morbidity in this high-risk cohort.[1-4] However, the alternative strategies for the management of these patients have been even more disappointing. Conservative medical treatment has been shown to have dismal outcomes,[11,12] whereas percutaneous coronary interventions, despite high procedural success rates, have been shown to be associated with increased incidence of restenosis needing repeat revascularization and high short- and long-term morbidity and mortality.[2,3,11-14] Although there is no randomized clinical trial that has evaluated the optimal revascularization strategy in patients with renal dysfunction, multiple observational studies have consistently shown that overall outcomes are better with CABG than with percutaneous coronary interventions.[2,3,12,13,15,16]

Our study adds to the growing evidence that patients with preoperative renal dysfunction in patients undergoing CABG represent a distinct group with increased comorbid conditions and are at higher risk of both short- and 2-year clinical adverse events. Death, pneumonia, acute renal failure, and need for dialysis featured prominently among the short-term risks associated with preoperative renal dysfunction, whereas the composite of death or MI were significantly increased at 2 years among patients with preoperative renal dysfunction than in those without preoperative renal dysfunction.

A number of mechanisms have been proposed to explain the propensity for worse clinical outcomes in patients with preoperative renal dysfunction.[17] These factors include greater comorbid conditions, lower use of evidence-based therapies (aspirin, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins), greater incidence of complications, and accelerated atherosclerosis. Our findings provide important insights into understanding the contributions of these factors in the attendant risks of patients with renal dysfunction undergoing CABG. Our data suggest that some, but not all, of these factors are operative in the heightened risks of these patients. Clearly, the increased comorbid conditions associated with preoperative renal dysfunction account considerably for their worse outcomes after CABG, as suggested by

TABLE 4. Clinical events through 30 days

Clinical events	Overall (n = 2973)	No renal dysfunction (n = 2533)	Preoperative renal dysfunction (n = 330)	*P* value
Death	1.2% (35)	0.9% (23)	2.7% (12)	.0011
Atrial fibrillation	26.0% (774)	25.3% (640)	30.5% (134)	.0221
Bleeding requiring reoperation	2.5% (74)	2.3% (58)	3.6% (16)	.0942
Pneumonia	2.3% (69)	2.1% (52)	3.9% (17)	.0199
Stroke	1.6% (46)	1.4% (35)	2.5% (11)	.0794
Adult respiratory distress syndrome	0.9% (25)	0.8% (20)	1.1% (5)	.4622
Mediastinitis	0.7% (21)	0.8% (20)	0.2% (1)	.1936
Pulmonary embolism	0.6% (17)	0.6% (16)	0.2% (1)	.2991
Perioperative MI	9.8% (291)	9.6% (243)	10.9% (440)	.3913
Postoperative acute renal failure	3.3% (98)	2.4% (60)	8.6% (38)	<.0001
Postoperative dialysis	0.6% (17)	0.4% (10)	1.6% (7)	.0021

MI, Myocardial infarction.

TABLE 5. Two-year major adverse clinical events

Clinical events	Preoperative renal dysfunction		Unadjusted		Adjusted*	
	No (n = 2533)	Yes (n = 440)	Hazard ratio (95% CI)	*P*	Hazard ratio (95% CI)	*P*
Death, MI (including perioperative MI), or revascularization						
No. of events	569	121	1.26	.0193	1.19	.1240
2-y event rate	22.6%	27.6%	(1.04–1.54)		(0.97–1.50)	
Death or MI (including perioperative MI)						
No. of events	350	98	1.65	<.0001	1.3	.0249
2-y event rate	13.8%	22.3%	(1.32–2.06)		(1.04–1.72)	
Death or revascularization						
No. of events	360	78	1.30	.0381	1.18	.2253
2-y event rate	14.3%	17.8%	(1.01–1.66)		(0.90–1.55)	
Death						
No. of events	93	44	2.83	<.0001	1.47	.0653
2-y event rate	3.7%	10.0%	(1.98–4.05)		(0.98–2.21)	

CI, Confidence interval; *MI,* myocardial infarction, *adjusted for age, gender, congestive heart failure, MI within 30 days of enrollment and use of ITA conduit.

significant attenuation of the risk of the outcomes on multivariable adjustments for these confounders. The increased postoperative morbidities (pneumonia, atrial fibrillation, postoperative acute renal failure, and need for dialysis, and the trend for increased incidence of postoperative bleeding and stroke) also seem to play an important role.

The use of evidence-based therapies did not differ significantly in patients with and without renal dysfunction undergoing CABG in our study. This is probably because the PREVENT-IV population may represent a highly select group already subjected to the most invasive coronary revascularization strategy (ie, CABG). Perhaps physicians are more concerned with preventing recurrent events in this cohort and less worried about the risks antecedent to the use of any evidence-based therapies. One notable exception was the lower use of ITA in patients with postoperative renal dysfunction. The use of ITA conduit in patients undergoing CABG has been shown to be associated with better short- and long-term outcomes[18] and is now considered a marker of quality of care provided by health care institutions for patients undergoing CABG.[19] Certainly this factor potentially influenced the short- and 2-year adverse clinical events among patients in our study as suggested by some attenuation of the risk of these events on risk adjustment. Nonetheless, this did not account completely for all of the increased risk of adverse clinical events in the current cohort, and preoperative renal dysfunction remained an important independent correlate of these events at follow-up. This and other previous investigations[1-3] suggest that differences in evidence-based therapies seem to have small yet definite effects on the differential risks of patients with and without preoperative renal dysfunction undergoing CABG. Thus, improving evidence-based care and increasing the use of ITA conduits in patients with preoperative renal dysfunction undergoing CABG represent important strategies for improving their outcomes.

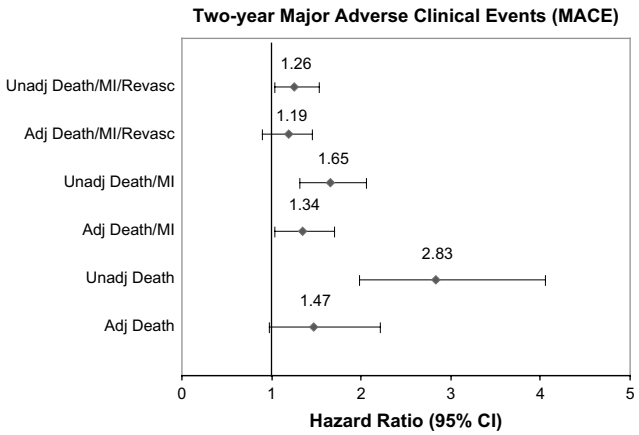

FIGURE 2. Unadjusted and adjusted graft failure rates in patients with preoperative renal dysfunction compared with those with no preoperative renal dysfunction. Small number of events precluded adjustments for ITA groups.

Most important, we found no difference in incidence of SVG or ITA failure and repeat revascularization in the 2 cohorts, a finding not demonstrated in any previous study. Furthermore, in those with similar quality of coronary arteries to which the grafts were anastomosed (categorized as good, fair, and poor), the failure rates of grafts did not differ. Thus, on the basis of our data, SVG or ITA failure or repeat revascularization of these conduits (markers of accelerated atherosclerosis) seemed to be similar among all patients undergoing CABG and less influenced by preoperative renal dysfunction. Thus, SVG and ITA failure is less likely to have a significant influence on the increased morbidity and mortality seen among patients with preoperative renal dysfunction undergoing CABG. Finally, treatment assignment (edifoligide vs placebo) had no differential effect on vein graft failure in patients with and without renal dysfunction.

Strength and Limitations

Our investigation should be viewed in the light of its strength and limitations. This is the first study to

prospectively collect not only clinical but also angiographic data that allowed assessment of SVG or ITA graft failure and repeat revascularization. This clinical and angiographic data permitted important insight into the mechanisms underlying the worse outcomes observed in patients with preoperative renal dysfunction undergoing CABG. However, this is a retrospective observational analysis of the PREVENT-IV data and limits inference regarding causation. Nonetheless, a large observational study such as this can be informative and hypothesis generating. Patients on dialysis were not excluded. However, patients with moderate to severe renal dysfunction may have been excluded from the PREVENT-IV study because of the need for angiographic follow-up. In addition, in the angiographic cohort, fewer patients with renal dysfunction underwent scheduled angiography. This was partly because patients with renal dysfunction were more likely to die before angiography. Unfortunately, we are unable to determine the rates of graft failure among patients who did not have follow-up angiography, potentially biasing our results. When we assumed that all deaths were associated with vein graft failure, however, we still found no significant in vein graft failure between patients with and without renal dysfunction. Follow-up beyond 2 years may provide additional information, and efforts are ongoing to collect this information. Finally, our findings are applicable to patients undergoing CABG and have limited generalizability to other patients with cardiovascular disease and renal dysfunction.

CONCLUSIONS

We found that patients with preoperative renal dysfunction have an increased risk of adverse short-term and 2-year clinical events after CABG. These data provide further insight into the factors influencing the risk of worse outcomes that include worse comorbidities, more post-CABG complications, and lower use of ITA with relative lesser impact of SVG or ITA failure. Further studies are needed to identify additional mechanisms of these worse outcomes and to evaluate appropriate measures that can improve the outcomes of patients with preoperative renal dysfunction undergoing CABG.

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